Original Article

Pulmonary Embolism: A Frequent Occurrence in Indian Patients with Symptomatic Lower Limb Venous Thrombosis

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OBJECTIVE: Pulmonary embolism (PE) is the most severe complication of deep venous thrombosis (DVT). There have been very few studies to assess the prevalence of PE in Asian patients. The objective of this study was to define the prevalence of PE in patients presenting with suspected lower limb DVT.

METHODS: This was a prospective cohort study at Sir Ganga Ram Hospital, a large multispecialty hospital in New Delhi, India. From January 2001 to July 2004, 1,552 consecutive inpatients and outpatients who presented with clinically suspected lower limb DVT were enrolled in the study. Combined ascending radionuclide venography and lung perfusion scan was performed in all patients. Patients with evidence of pulmonary perfusion defects underwent ventilation lung scan.

RESULTS: Radionuclide venography-detectable DVT was noted in 744 patients, of whom 521 (70%) had suprapopliteal DVT. Of patients with DVT, 294 (39.5%) showed a high-probability lung scan and 135 (18.1%) had an intermediate-probability lung scan. Overall, 47% of patients with a high-probability scan had no clinical manifestations suggestive of PE.

CONCLUSION: PE occurs frequently in Indian patients with symptomatic DVT. Increasing awareness will provide us with clearer ideas about the prevalence of venous thromboembolism in Asian countries. [*Asian J Surg* 2006;29(2):86–91]

Key Words: Asian, complication, deep venous thrombosis, prevalence, pulmonary embolism

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Introduction

Pulmonary embolism (PE) is the most severe complication of deep venous thrombosis (DVT). Both conditions produce few specific symptoms and signs, hence, clinical diagnosis is unreliable.[1] The manifestation spectrum of PE ranges from silent to a massive, sometimes suddenly fatal, event. Prompt diagnosis and appropriate treatment of this condition can dramatically reduce its attendant mortality and morbidity.

In patients with DVT, a clinical dilemma arises because a large number of patients with PE do not present with the classical symptoms and signs. The need for anticoagulation necessitates objective testing to confirm or exclude these diagnoses. It has been proven previously that proximal venous thrombosis is associated with a high prevalence of PE.[2–4]

PE carries a significant risk of mortality. Nearly 10% of patients who die of PE do so within 1 hour of the onset of symptoms.[5] The few population-based studies have demon-

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strated an average annual incidence of DVT and PE of 48 and 23 per 100,000 persons, respectively.[6,7]

The detection of silent PE in patients with DVT is of prime importance, especially when outpatient treatment is considered.[8,9] Ventilation-perfusion lung scanning is a highly sensitive, noninvasive method to detect PE.[10,11] The accuracy is further improved by combining perfusion scanning with clinical assessment. Based on the hypothesis that DVT and PE are separate but related components of a larger syndrome (venous thromboembolism, VTE), we performed radionuclide venography and ventilation-perfusion lung scanning in all consecutive patients with clinically suspected DVT to determine the prevalence of PE.

Patients and methods

Patients

Between January 2001 and July 2004, consecutive in- and outpatients presenting with clinically suspected lower limb DVT were enrolled in the study. Patients were eligible if they were aged 18 years or older. A combination radionuclide ascending venography with lung perfusion scan was performed within 24 hours of presentation at the Department of Nuclear Medicine.

Radionuclide venography

Radionuclide venography was performed following slow infusion of 4–6 mCi of 99m technetium (Tc)-labelled albumin macroaggregates into the dorsal pedal veins of both feet. Tourniquets were applied tightly bilaterally at three levels (above ankle, below knee and at mid thigh). The transit of tracer was assessed simultaneously in the anterior and posterior projections. Dynamic whole-body imaging was conducted with a dual-head variable-geometry gamma camera, using a high-resolution parallel-hole collimator.

Perfusion scan

A lung perfusion scan was performed immediately after radionuclide venography. A minimum of four views (anterior, posterior, and right and left lateral oblique) were acquired on a 256 × 256 matrix, using a parallel-hole high-resolution collimator with a minimum of 500,000 counts.

Ventilation scan

A ventilation scan was obtained if there was any abnormality on the lung perfusion scan. The patient was nebulized using 99m Tc-labelled diethylenetriaminepentaacetic acid aerosol immediately before lung images were obtained using a parallel-hole high-resolution collimator with a minimum of 200,000 counts. At least four views were acquired.

Interpretation of radionuclide venography

Two independent experienced nuclear medicine physicians analysed the images. The following criteria were used to diagnose DVT:[12] no or poor visualization of a vein, visualization of collateral veins, visualization of superficial veins in the absence of deep veins and pre-obstruction accumulation of tracer (pooling).

Interpretation of radionuclide lung scans

The lung perfusion and ventilation scans were evaluated using the Prospective Investigation of PE Diagnosis (PIOPED) criteria.[10] Scan defects were classified into high, intermediate or low probability of PE or normal scan.

Results

A total of 1,552 consecutive in- and outpatients (618 males, 934 females; mean age, 42 years; age range, 24–65 years) with clinically suspected lower limb DVT were enrolled in the study. Most patients (1,314; 84.7%) presented on an outpatient basis.

Swelling of the lower limbs was the most common presenting symptom of DVT (Table 1). Many patients presented with a combination of symptoms. Additional symptoms suggestive of PE, such as breathlessness, chest discomfort, chest pain and haemoptysis, were found in only 251 (16.2%) patients. Haemodynamic instability (systolic blood pressure < 100 mmHg, poor peripheral tissue perfusion) was evident in 28 (1.8%) patients.

Of the 1,552 patients, 744 had DVT detected by radionuclide venography, 183 (24.6%) in both lower limbs. Many

Table 1. Presenting symptoms in patients with suspected deep venous thrombosis (DVT)

Symptom	*n*
Pain in lower limb	603
Swelling of lower limb	1,328
Swelling and pain	518
Breathlessness	103
Chest tightness/discomfort	94
Chest pain	42
Haemoptysis	12
Hypotension	28

(70%) had proximal (suprapopliteal) DVT, which was subdivided into infrainguinal (femoropopliteal) or suprainguinal (iliofemoral) DVT. Among patients with radionuclide venography-proven DVT, a high-probability lung scan was noted in 294 (39.5%) (Table 2). In contrast, in patients without radionuclide detectable DVT, the prevalence of a high-probability lung scan was 4.5% ($p < 0.001$, chi-square).

The prevalence of lung scan defects in patients with or without symptoms suggestive of PE is shown in Table 3. Nearly half of patients with a high-probability lung scan had no symptoms suggestive of PE.

Table 4 shows the distribution of lung scan defects according to the site of DVT. A higher prevalence of PE was noted in patients with suprapopliteal DVT than those with popliteal vein thrombosis. The overall prevalence of PE in patients with DVT was 39.5%. The PE prevalence in patients with popliteal, infrainguinal and suprainguinal DVT was 23%, 42% and 52%, respectively.

The mortality rate in patients with DVT was 0.95% (6 patients with a high-probability scan and 1 with an intermediate-probability scan).

Discussion

PE and DVT are separate but related aspects of the same dynamic disease process, now termed VTE.[13,14] An increasing volume of Western literature has confirmed that PE occurs frequently in patients with DVT.[2–4,15,16] However, literature from Asia has shown a wide variation in the incidence of DVT and VTE. In their systematic review, Liew et al suggested that, in spite of the variation in the reported occurrence of VTE, this disease is not as rare in Asia as was thought previously.[17] The common occurrence of DVT in Asian patients has also been reported in other hospital-based studies.[18,19] However, a recent population-based study by Cheuk et al noted that VTE is not as common in Chinese as in Caucasians.[20]

Table 2. Results of radionuclide lung scan

	Patients with proven DVT	Patients with no DVT
V/Q scan result		
Normal	305 (42%)	701 (86.8%)
Low probability	18 (1.5%)	45 (5.5%)
Intermediate probability	127 (17%)	26 (3.2%)
High probability	294 (39.5%)	36 (4.5%)

V/Q = ventilation/perfusion; DVT = deep venous thrombosis.

Table 3. Prevalence of lung scan defects in patients

	Patients with DVT	Patients with no DVT
Lung scan defects		
Low probability	18 (7)	45 (6)
Intermediate probability	127 (48)	26 (10)
High probability	294 (158)	36 (22)

The numbers in parentheses denote the numbers of patients with symptoms suggestive of pulmonary embolism. DVT = deep venous thrombosis.

Table 4. Correlation between site of deep venous thrombosis (DVT) and lung scan defects

	n	Intermediate probability	High probability
Site of DVT			
Popliteal	223	16	54 (23%)
Suprapopliteal	521	111	240 (46%)
Infrainguinal	314	65	132 (42%)
Suprainguinal	207	46	108 (52%)

Table 5. Reported prevalence of pulmonary embolism (PE) in patients with deep venous thrombosis (DVT)

Authors	Diagnostic modality	DVT, *n*	PE, *n* (% prevalence)
Huisman et al[2]	Venography, V/Q scan	89	45 (51%)
Moser et al[3]	Venography, pulmonary angiography	44	23 (52%)
Meignan et al[4]	Venography, V/Q scan	622	309 (49.5%)
Monreal et al[15]	Venography, V/Q scan	116	29 (25%)
Borst-Krafek et al[16]	Duplex, V/Q scan	212	(42–51%)*
Present study	Radionuclide venography with V/Q scan	744	294 (39.5% overall) (23–52%)*

*Site-specific prevalence (popliteal, suprapopliteal or suprainguinal DVT). V/Q = ventilation/perfusion.

Our hospital-based data confirm that PE is indeed a frequent condition in patients with symptomatic lower limb DVT. The rationale for using combination radionuclide ascending venography and lung perfusion scan was the simultaneous assessment of both peripheral (venous) and pulmonary thromboembolism. Reports assessing the accuracy of radionuclide venography have shown that it compares well with contrast venography, especially for popliteal and suprapopliteal DVT.[12,21] The sensitivity and specificity in the infrapopliteal segment, however, is slightly lower.[21] In the current duplex era, this single test gives accurate, reliable and operator independent information.

The prevalence of high-probability lung scans in patients with DVT was nearly 40% in our study, which is similar to the reports of other investigators who used scintigraphy or angiography to document PE.[2–4,15] Table 5 compares the prevalence of PE in previously published reports and the present study. Considering that in patients with a non-high probability scan, pulmonary angiography can confirm emboli in approximately 30%,[22] the true prevalence of PE may be higher. Clinical symptoms suggestive of PE were noted in 158 (53%) patients with DVT with a high-probability lung scan. Thus, approximately half of patients had a silent PE documented on lung perfusion scan.

Detection of silent PE in patients with DVT has important implications, especially when outpatient treatment is considered. Home-administered low-molecular-weight heparin (LMWH) and subcutaneous heparin are as efficacious as intravenous unfractionated heparin administered in hospital.[23] Considering the benefits in terms of avoidance of hospital stay and no need for monitoring, we advocate the home-based use of LMWH followed by oral anticoagulation for patients with DVT. Patients with DVT and no evidence of PE were safely managed on an outpatient basis and treated with LMWH. Those with high- and intermediate-probability lung scans were admitted and their treatment protocol is outlined in Figures 1 and 2.

The other advantage of obtaining a baseline lung scan in patients with DVT is that it serves as a comparison when a repeat scan is performed on later suspicion of PE. Hence,

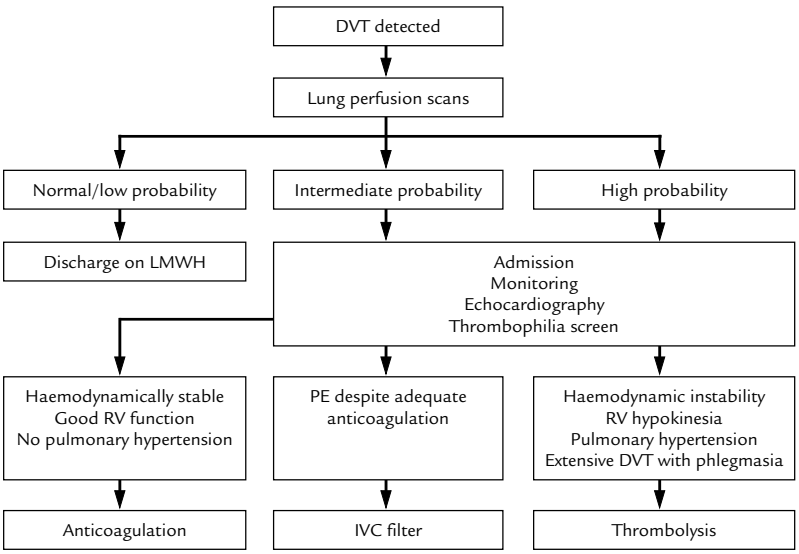

Figure 1. Management protocol for patients with radionuclide venography-detected deep venous thrombosis (DVT). LMWH = low-molecular-weight heparin; RV = right ventricular; PE = pulmonary embolism; IVC = inferior vena cava.

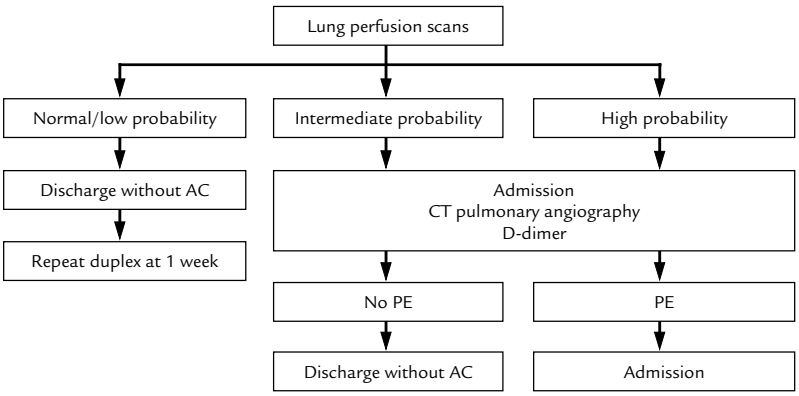

Figure 2. Treatment protocol for patients with no deep venous thrombosis (DVT) on radionuclide venography. AC = anticoagulation; CT = computed tomography; PE = pulmonary embolism.

perfusion defects detected before initiation of treatment would not be interpreted later as therapeutic failure. Fresh lung scan defects in a patient on adequate anticoagulation may be an indication for inferior vena cava filter placement.

The detection of PE at such a high frequency should not produce a dramatic change in management. Evidence has shown no major benefit of thrombolytic therapy over standard anticoagulation therapy in terms of mortality, recurrent PE or chronic complications.[24] Hence, thrombolysis is used only in situations where it is truly indicated.[24,25] The absolute indication for thrombolysis is massive PE with haemodynamic instability. Evidence of right ventricular hypokinesia or raised pulmonary artery systolic pressure (> 50 mmHg) are also considered to be relative indications for thrombolysis in haemodynamically stable patients. Extensive DVT, especially with phlegmasia alba or dolens, may also be managed using thrombolytic therapy to achieve more complete clot lysis. LMWH is as safe and effective as unfractionated heparin and can be used in carefully selected patients with clinically stable PE.[26] However, we prefer to hospitalize patients with PE and monitor them for a few days during anticoagulation therapy.

In conclusion, our study reveals a high prevalence of PE in Indian patients presenting with symptomatic lower limb DVT. These findings confirm the need for increased awareness of VTE in Asian populations. This high prevalence compares well with the previously reported rate of PE in Western patients with DVT. Further studies are needed to determine the cost-effectiveness of such single diagnostic tools for the diagnosis of both DVT and PE.

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